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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Feder *et al.*

Application No.: To be assigned

Group Art Unit: 1653

Filed: Herewith

Examiner: Gupta, A.

For: PEPTIDES AND PEPTIDE ANALOGUES DESIGNED FROM HFE PROTEIN AND THEIR USES IN THE TREATMENT OF IRON OVERLOAD DISEASES

Attorney Docket No.: 8907-091-999

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examining the captioned application on the merits, please enter the following amendments and consider the following remarks.

AMENDMENT

IN THE CLAIMS

Please cancel Claims 1-13, without prejudice, and insert therefor the following new Claims 14-19:

--14. (New) A method of inhibiting TfR binding to transferrin, comprising administering to a subject a therapeutically effective amount of a compound comprising the formula:

(I) Z_1-X_1-X_2-X_3-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}-X_{11}-X_{12}-X_{13}-X_{14}-X_{15}-X_{16}-X_{17}-Z_2

wherein:

X_1 is an apolar residue;

X_2 is a hydrophobic residue;

X_3 is an acidic or an aliphatic residue;

X_4 is a basic residue;

X_5 is an apolar residue;

X_6 is an aromatic residue;

X_7 is a polar residue;

X_8 is an aliphatic residue;

X_9 is an acidic or an aliphatic residue;

X_{10} is an aromatic residue;

X_{11} is an aromatic residue;

X_{12} is a polar residue;

X_{13} is Ile;

X_{14} is an apolar residue;

X_{15} is an acidic residue;

X_{16} is a polar residue;

X_{17} is a basic or an aliphatic residue;

Z_1 is H_2N-, RHN- or, RRN-;

Z_2 is -C(O)R, -C(O)OR, -C(O)NHR, -C(O)NRR;

each R is independently (C_1-C_6) alkyl, (C_1-C_6) alkenyl, (C_1-C_6) alkynyl, substituted (C_1-C_6) alkyl, substituted (C_1-C_6) alkenyl or substituted (C_1-C_6) alkynyl;

each "—" between residues Z_1 and X_1 and residues Z_2 and X_{17} represents a covalent linkage; and

each "—" between residues X_1 through X_{17} represents a covalent linkage,

wherein the compound reduces cell-associated binding of transferrin as measured in an *in vitro* cellular binding assay and produces at least an additive effect with soluble HFE/β_2m heterodimers in reducing cell-associated binding of transferrin as measured in the assay.

15. (New) The method of Claim 14, wherein:

X_1 is an apolar amino acid;

X_2 is an aromatic amino acid;

X_3 is an acidic amino acid;

X_4 is a basic amino acid;

X_5 is an apolar amino acid;

X_6 is an aromatic amino acid;

X_7 is a polar amino acid;

X_8 is a aliphatic amino acid;

X_9 is a an acidic amino acid;

X_{10} is an aromatic amino acid;

X_{11} is an aromatic amino acid;

X_{12} is a polar amino acid;

X_{13} is Ile;

X_{14} is an apolar amino acid;

X_{15} is an acidic amino acid;

X_{16} is a polar amino acid;

X_{17} is a basic amino acid; and

each "—" between residues X_1 through X_{17} is independently an amide, a substituted amide or an isostere of amide.

16. (New) The method of Claim 14, wherein:

X_1 is Gly;

X_2 is Trp or Ala;

X_3 is Asp or Ala;

X_4 is His;

X_5 is Met;

X_6 is Phe;

X_7 is Thr;

X_8 is Val;

X_9 is Asp or Ala;

X_{10} is Phe;

X_{11} is Trp;

X_{12} is Thr;

X_{13} is Ile;

X_{14} is Met;

X_{15} is Glu;

X_{16} is Asn;

X_{17} is His or Ala;

Z_1 is H_2N-;

Z_2 is -C(O)OH; and

each "—" between residues X_1 through X_{17} is an amide linkage.

17. (New) A method of treating an iron overload disease, comprising administering to a subject a therapeutically effective amount of a compound comprising the formula:

(I) Z_1-X_1-X_2-X_3-X_4-X_5-X_6-X_7-X_8-X_9-X_{10}-X_{11}-X_{12}-X_{13}-X_{14}-X_{15}-X_{16}-X_{17}-Z_2

wherein:

X_1 is an apolar residue;

X_2 is a hydrophobic residue;

X_3 is an acidic or an aliphatic residue;

X_4 is a basic residue;

X_5 is an apolar residue;

X_6 is an aromatic residue;

X_7 is a polar residue;

X_8 is an aliphatic residue;

X_9 is an acidic or an aliphatic residue;

X_{10} is an aromatic residue;

X_{11} is an aromatic residue;

X_{12} is a polar residue;

X_{13} is Ile;

X_{14} is an apolar residue;

X_{15} is an acidic residue;

X_{16} is a polar residue;

X_{17} is a basic or an aliphatic residue;

Z_1 is H_2N-, RHN- or, RRN-;

Z_2 is -C(O)R, -C(O)OR, -C(O)NHR, -C(O)NRR;

each R is independently (C_1-C_6) alkyl, (C_1-C_6) alkenyl, (C_1-C_6) alkynyl, substituted (C_1-C_6) alkyl, substituted (C_1-C_6) alkenyl or substituted (C_1-C_6) alkynyl;

each "—" between residues Z_1 and X_1 and residues Z_2 and X_{17} represents a covalent linkage; and

each "—" between residues X_1 through X_{17} represents a covalent linkage,

wherein the compound reduces cell-associated binding of transferrin as measured in an *in vitro* cellular binding assay and produces at least an additive effect with soluble HFE/β_2m heterodimers in reducing cell-associated binding of transferrin as measured in the assay.

18. (New) The method of Claim 17, wherein:

X_1 is an apolar amino acid;

X_2 is an aromatic amino acid;

X_3 is an acidic amino acid;

X_4 is a basic amino acid;

X_5 is an apolar amino acid;

X_6 is an aromatic amino acid;

X_7 is a polar amino acid;

X_8 is a aliphatic amino acid;

X_9 is a an acidic amino acid;

X_{10} is an aromatic amino acid;

X_{11} is an aromatic amino acid;

X_{12} is a polar amino acid;

X_{13} is Ile;

X_{14} is an apolar amino acid;

X_{15} is an acidic amino acid;

X_{16} is a polar amino acid;

X_{17} is a basic amino acid; and

each "—" between residues X_1 through X_{17} is independently an amide, a substituted amide or an isostere of amide.

19. (New) The method of Claim 17, wherein:

X_1 is Gly;

X_2 is Trp or Ala;

X_3 is Asp or Ala;

X_4 is His;

X_5 is Met;

X_6 is Phe;

X_7 is Thr;

X_8 is Val;

X_9 is Asp or Ala;

X_{10} is Phe;

X_{11} is Trp;

X_{12} is Thr;

X_{13} is Ile;

X_{14} is Met;

X_{15} is Glu;

X_{16} is Asn;

X_{17} is His or Ala;

Z_1 is H_2N-;

Z_2 is -C(O)OH; and

each "—" between residues X_1 through X_{17} is an amide linkage.--

REMARKS

With this Amendment, Claims 1-13 have been canceled, without prejudice, and replaced with new Claims 14-19. Applicants expressly reserve the right to prosecute claims drawn to the canceled subject matter in one or more timely filed continuation, divisional or continuation-in-part applications. New Claims 14-19 merely recite with greater particularity and/or clarity certain features of canceled Claims 8-13.

As demonstrated by the table below, new Claims 14-19 are fully supported by the application and claims as originally filed and do not constitute new matter. Entry into the instant application is therefore proper and kindly requested. Specific support for each new claim is provided in the following table:

New Claim	Support (original Claim; page (line nos.))
14	Claim 8; 7 (10) through 8 (1); 20 (32-34); 26 (6) through 27 (4)
15	Claim 9; 14 (18) through 15 (5); 20 (32-34)
16	Claim 10; 15 (6-29); 20 (32-34)
17	Claim 11; Claim8; 7 (10) through 8 (1); 20 (32) through 21 (3)
18	Claim 12; 14 (18) through 15 (5); 20 (32) through 21 (3)
19	Claim 13; 15 (6-29); 20 (32) through 21 (3)

CONCLUSION

New Claims 14-19 are believed to be in condition for allowance. An early indication of the same is kindly solicited.

No fees are believed due in connection with this submission. However, the Commissioner is authorized to charge any required fees, or credit any overpayment, to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

Date July 9, 2001

47,763
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Enclosure

New Claim	Support (original Claim; page (line nos.))
14	Claim 8; 7 (10) through 8 (1); 20 (32-34); 26 (6) through 27 (4)
15	Claim 9; 14 (18) through 15 (5); 20 (32-34)
16	Claim 10; 15 (6-29); 20 (32-34)
17	Claim 11; Claim8; 7 (10) through 8 (1); 20 (32) through 21 (3)
18	Claim 12; 14 (18) through 15 (5); 20 (32) through 21 (3)
19	Claim 13; 15 (6-29); 20 (32) through 21 (3)

CONCLUSION

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Enclosure

Transfer Request

application. A duplicate copy of this sheet is enclosed for filing in the prior application file.

4b. ☐ New formal drawings are enclosed.

4c. ☒ Drawings are enclosed.

5a. ☒ Priority of application no. 09/216,077 filed on December 18, 1998 in the United States is claimed under 35 U.S.C. §120.

5b. ☐ The certified copy has been filed in prior application no. , filed .

6. ☒ The prior application is assigned of record to Bio-Rad Laboratories, Inc. and the California Institute of Technology.

7a. ☒ The Power of Attorney appears in the prior application no. 09/216,077 filed December 18, 1998.

7b. ☐ Since the Power of Attorney does not appear in the original papers, a copy of the Power in prior application no. , filed is enclosed.

8. ☒ This application contains nucleic acid and/or amino acid sequences required to be disclosed in a Sequence Listing under 37 CFR §§1.821-1.825. It is requested that the Sequence Listing in computer readable form from prior application no. 09/216,077, filed on December 18, 1998 be made a part of the present application as provided for by 37 C.F.R. §1.821(e). The sequences disclosed therein are the same as the sequences disclosed in this application. A copy of the paper Sequence Listing from application no. 09/216,077 is enclosed.

9. ☒ The undersigned states, under 37 C.F.R. §1.821(f), that the content of the enclosed paper Sequence Listing from application no. 09/216,077 is the same as the content of the computer readable form submitted in application no. 09/216,077.

10. ☒ A copy of the application and signed Declaration from the application no. 09/216,077 is enclosed.

11. ☒ A copy of the Information Disclosure Statements with revised form PTO 1449 from application no. 09/216,077 are enclosed. Copies of the references cited can be found in application no. 09/216,077. The Examiner is respectfully requested to transfer the references to the instant application and that these references be made a part of the file history of the instant application.